Remarks

Claims 1, 4-6, 12, 13, 15, 17, 20, 7, 71, 73-89, 91, 118-119, 153-181 are pending in this application. Claims 2, 3, 7-11, 16, 18, 19, 27-67, 90, and 92-117 have been previously canceled. Claims 14, 68-72, 90, and 120 are presently canceled. Claims 21-26, and 121-152 have been previously withdrawn. Applicants reserve the right to pursue the subject matter of the withdrawn or canceled claims in one or more continuation or divisional applications.

Claims 1, 13, 20, 73 and 91 are herein presently amended.

Claims 1 and 20 have been amended to define and limit the aptamer of the current invention to those that include an RNA aptamer that binds to Factor IXa and has a first stem region, a first loop region, a second stem region, a second loop region, and a third loop region, in which the first loop region has a consensus sequence comprising NNAUA, wherein N is selected from the group consisting of A, U, G, and C. Support for the amendments can be found on pages 24-25 of the application, which describes the secondary structure of the particular RNA aptamers of the current invention, as well as the consensus sequence.

Claim 13 has been amended to conform with the Examiner's restriction requirement.

Claim 73 has been amended to depend from a pending claim (claim 12), as well as to replace the term ribonucleotide with nucleotide.

Claim 91 has been amended to define the location on the aptamer of the described nucleotides. Support for the amendment can be found on pages 24-25 of the application, which describes the secondary structure of the particular RNA aptamers of the current invention.

Claim 153-181 have been newly added. New claim 153 is dependent on claim 1. Support for new claim 153 can be found on page 23, line 20.

New claims 154-155 are dependent on claim 20. Support for the new claims can be found on pages 23-25 of the application.

New claim 156 is an independent claim to RNA aptamers which are at least 80% homologous to Seq. ID. NOs: 3 and 70, or a truncate thereof. Support for the new claim can be found on page 22, line 27-page 23, line 7. New claims 157-179 are dependent on claim 156.

New claim 180 is an independent claim to a pharmaceutical composition comprising RNA aptamers which are at least 80% homologous to Seq. ID. NOs: 3 and 70, or a truncate

thereof. Support for the new claim can be found on page 22, line 27-page 23, line 7. New claim 181 is dependent on claim 180.

35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 1-6, 12, 20-26, 68-91, 119 and 120 over 35 U.S.C. § 112, first paragraph because the Examiner alleges that the specification does not contain adequate written description to support these claims.

The Examiner first alleges that the specification only provides support for RNA aptamers, not nucleic acid aptamers as recited in the claims. In response to the Examiner's rejection, the Applicants have amended the claims to clearly refer to RNA aptamers. Support for this amendment is found on page 5, lines 8-10, as well as throughout the specification.

The Examiner also alleges that the specification does not provide adequate written description to support the full genus of aptamers to Factor IXa. The Examiner suggests that the specification does not provide a teaching of what nucleic acid sequences or secondary structures would be or would have been expected for these aptamers. The Examiner suggests that aptamers described in the specification are of different secondary structure where there is no disclosed core structure that imparts the function of binding to factor IXa as a nucleic acid aptamer.

In response to the Examiner's rejection, the Applicants have limited the claims to RNA aptamers that have a secondary structure including a first stem region, a first loop region, a second stem region, a second loop region, and a third loop region, wherein the first loop region includes a consensus sequence comprising NNAUA, wherein N is selected from the group consisting of A,U,G, and C. Support for the amendments can be found on pages 24-25 of the application, which describes the secondary structure of the particular RNA aptamers of the current invention, as well as the consensus sequence.

The claims as currently amended provide for structural limitations that correlate with the functional ability of the claimed aptamers to bind Factor IXa. In identifying aptamers that bind to Factor IXa, Applicants screened roughly 10^{14} sequences utilizing the methods described in the application. The phylogeny of aptamers identified that bind to Factor IXa have two conserved structural characteristics. First, the aptamers have a conserved secondary structural organization.

This common conformational secondary structure includes a first stem region, a first loop region, a second stem region, a second loop region, and a third loop region.

The second conserved structural characteristic is a conserved NNAUA consensus sequence located in the first loop region of the structure. This conserved sequence is common amongst the aptamers identified as binding to Factor IXa, strongly indicating that this conserved sequence, as well is its location within the secondary structure, is critical to binding. A canonical representation of the consensus secondary structure with the conserved consensus sequence located in the first loop region is provided in Figure 20.

Aptamer technology is a mature technology, and the level of skill of those which focus on this art is high and advanced. Given the secondary structural characteristics and consensus sequence provided for in the currently amended claims, as well as the amino acid sequence of the target protein Factor IXa, those skilled in the art can clearly envision the structure of the claimed aptamers.

As stated by the PTO Guidelines, the written description requirement can be met by "showing that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Guidelines, *66 Fed. Reg. at 1106.* In *Enzo Biochem, Inc. v. Gen-Probe Incorporated*, 296 F.3d 1316 (Fed. Cir. 2002) the Federal Circuit adopted the PTO's applicable guidelines on the written description requirement. At issue in the *Enzo* case was whether a claim to a composition of matter met the written description requirement of § 112, Para. 1 given the fact that the composition was described only with respect to its function, that function being its ability to hybridize in a favorable ratio to the DNA of a deposited bacterium. *Id.* at 1322 The Federal Circuit specifically stated that the "written description requirement would be met ...if the functional characteristics of preferential binding [of the nucleic acids]...were coupled with a disclosed correlation between that function and a structure that is sufficiently known or disclosed". *Id.* at 1325-1326. As described above, the currently amended claims provide for conserved structural characteristics that correlate with their functional ability to bind to Factor IXa. As amended, the current claims meet the applicable standards for written description.

Specification

Applicants have provided a Substitute Figure 18. In the originally filed Figure 18, several nucleotides in two of the listed sequences was inadvertently misplaced. For the sequence identified as 9-11, a C was inadvertently placed at the first 5' position in the last column labeled S1. The C should be in the column labeled L3.

In the sequence identified as 9-4, an A was inadvertently placed in the last 3' position of the first column labeled S1. The A should be the first 5' position in the column labeled L1. In addition, a U was inadvertently placed at the first 5' position in the last column labeled S1. The U should be in the column labeled L3.

Substitute Figure 18 corrects these misalignments. The Applicants respectfully request that substitute Figure 18 be herewith entered.

Restriction Requirement

Applicants acknowledge the Examiner's rejection of Applicants' grounds of traversal with respect to Group IV.

In the Office Action response of February 2, 2004, Applicants stated that "Suggesting that an experimental setting is a materially different method from the therapeutic use is a suggestion that an *in vitro* model is a wholly different invention from the disease it is modeling... In this case, an *in situ* hybridization is nothing more than a research model of what occurs in the blood stream *in vivo*." Applicants wish to clarify this statement by indicating that the statement was not meant to suggest that methods describing *in vitro* diagnostic applications should be viewed as describing or enabling methods of *in vivo* therapeutic applications. Applicants refer the Examiner to the Office Action response filed on March 23, 2006 in related case 10/155,233 for Applicants' views on this issue.

Applicants believe no further fees are due with this response. Should the Examiner determine otherwise, the Commissioner is hereby authorized to debit any required fee from Deposit Account 11-0980.

Respectfully submitted,

w/express permission

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